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REVIEW ARTICLE

A human papillomavirus public vaccination program in Taiwan: The Kinmen County experience

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In Taiwan, cervical cancer is ranked sixth among all causes of death in women. With the goal of reducing the incidence of cervical cancer, the Kinmen County Health Bureau planned to implement a pilot human papillomavirus (HPV) vaccination program in 2007. The Bureau established a committee to promote public awareness, coordinate with the schools, arrange for the administration of the vaccine, establish a vaccination registry, and develop a plan for follow-up and assessment. Vaccination for female residents aged 16–18 began through a school-based program in 2008. A total of 1633 girls completed the vaccination protocol within 3 years, and vaccine uptake rates of over 90% were achieved by 2010. No serious adverse events were reported among those who were vaccinated. The experience gained from the Kinmen County HPV vaccination program has helped and will continue to help establish an operational model for similar programs throughout the country.

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Introduction

In Taiwan, cervical cancer is ranked sixth among all causes of death in women, and is the second most frequent cancer

in women aged 15–44.¹ In 1995, the Bureau of Health Promotion initiated a national program of annual Pap screening for all women over 30 years of age and a national Pap smear registry was established. The screening program has resulted in a decrease in the age-standardized incidence rate for invasive cervical cancer from 24 cases per 100,000 women in 1995 to fewer than 13 cases per 100,000 women in 2006, and a marked decrease in the mortality rate from cervical cancer, from 11 deaths per 100,000 women in 1995 to 5.8 deaths per 100,000 women in 2007, a reduction of 46% and 47% in the incidence of cervical cancer and its mortality, respectively.²

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In the early 1980s, researchers discovered an association between certain strains of human papillomavirus (HPV) and cervical cancer. In Taiwan, hospital-based HPV screening revealed that the most common types of HPV related to invasive cervical cancer were types 16, 18, 52, and 58.³

HPV vaccines, first approved in the United States in 2006, are expected to prevent an estimated 70% of future cervical cancer cases,^{4,5} as well as offer protection against other HPV-related cancers. Previous studies in Taiwan^{6–8} have concluded that vaccination is cost-effective in terms of future expenditures for health care and improvements in life expectancy. Although universal HPV vaccination will not reduce the incidence of cervical cancer in the short term, a decline in the number of cervical cancer cases is expected some decades from now.

Based on a population dynamic transmission model, a 91% reduction in HPV 16/18-related cervical cancers from vaccination was estimated to result in an incremental cost-effectiveness ratio of New Taiwan Dollar (NTD) 410,477 per quality-adjusted year of life gained from a vaccination program targeting women between ages 12 and 24.^{6,7} This result is considered to be cost-effective as it is less than the *per capita* gross domestic product of NTD 450,000 in 2007. Other studies have confirmed that vaccination is cost-effective for girls and young women.^{9,10}

Vaccine uptake is crucial to the success of a publicly funded HPV vaccination program. Several factors can affect the rate of public acceptance.^{11,12} These include public understanding that vaccination of a healthy person reduces the risk of that person contracting the disease, ease of access to vaccination, previous immunization experience, and parental concern over the sexual implications of HPV vaccination.¹³ This article provides an overview about the establishment and implementation of a public HPV vaccination program in Kinmen County, Taiwan.

Methods

The Kinmen County Health Bureau established an HPV program committee comprised of internal Bureau officers and external HPV vaccination-related experts to oversee the promotion of public awareness, collaboration with the schools, administration of the vaccine, establishment of a vaccination registry, and development of plans for follow-up and assessment.

Promotion of public awareness

A survey by Trim et al showed a high public acceptance rate for HPV vaccination, with the only major concern being vaccine safety.¹⁴ With existing comprehensive safety and efficacy data from placebo-controlled phase III studies in over 18,000 HPV vaccine recipients,^{15,16} the committee developed a communication strategy to disseminate this safety and efficacy information. The committee organized 11 educational events, inviting the general public, women's rights advocacy group leaders, health-care practitioners, government officials, and school teachers to participate in informational sessions led by gynecologic oncology experts. In addition, the committee developed a series of public awareness programs, including (1) interviews featuring

gynecologic oncologists and pediatric infection specialists broadcast on Kinmen County television stations; (2) public service messages featuring the voice of the chief of the Kinmen County Health Bureau broadcast on national radio programs; (3) school-based, face-to-face health education lectures; (4) posters and banners displayed in schools, health clinics, hospitals, and government offices; (5) large and frequent advertisements in Kinmen County newspapers. All of these efforts focused on educating the public about the prevalence of HPV, its role in the development of cancer, the safety of the vaccine, and the optimal age for vaccination. Details about the free vaccination program provided by the Kinmen County government were also provided.

Target population

A previous survey in Taiwan had indicated that girls' average age of becoming sexually active was 16.15 years and that 10.4% of adolescent girls were sexually active.¹⁷ Optimally, HPV vaccination should be completed before sexual activity starts; however, to avoid potential parental objection to vaccinating the very young cohort due to the sexual connotation of HPV vaccination, the Kinmen County Health Bureau established a 3-year vaccination program targeting all high-school girls between 16 and 18 years of age. This age group was targeted as the priority cohort because they needed to be protected more urgently than did the younger junior high-school cohort of 13–15 year olds. This cohort was also more readily accessible through a school-based network compared with the older catch-up cohort of women up to 26 years of age who could be accessed primarily through a community-based health-care network.

Vaccine administration

A vaccination schedule was constructed for the administration of the first, second, and third doses of the HPV vaccine in each high school in the county. Administration of the vaccine was carried out by qualified medical practitioners following the public vaccination standard procedure issued by the Centers for Disease Control, Taiwan. Body temperature was measured before vaccine administration. Those presenting with fever ($>38.5^{\circ}\text{C}$) or other signs of illness were not vaccinated and were instructed to receive vaccination from a primary health-care provider once the symptoms have subsided. Those who were vaccinated remained seated in the health station under the supervision of the physician and nurses for at least 30 minutes. Any adverse events reported by the vaccine recipient or observed by the practitioner were recorded and managed accordingly. A postvaccination educational card was given to each student who was vaccinated, which reminded them to report any event occurring during the next 7 days. The vaccine was administered free of charge to eligible recipients.

Assessments

The committee established a mandatory registry to document the name of the vaccine recipient, vaccination date,

Table 1 Vaccine uptake rates.

Year	Age of cohort (y)	Eligible vaccine recipients (n)	First dose uptake rate [% (n)]	Second dose uptake rate [% (n)]	Third dose uptake rate [% (n)]
2008	16–18	1438	66 (949)	64 (920)	63 (906)
2009	16	368	92 (339)	89 (328)	86 (317)
2010	16	379	91 (345)	91 (345)	89 (337)

vaccine batch number, and any adverse event occurring while administering the vaccine. This would enable the detection of short-term safety and tolerability issues and facilitate long-term follow-up.

To evaluate public perception of the program, a post-vaccination survey was mailed to the target population and their parents after the first pilot cohort was completed in 2008. The objective of the survey was to evaluate parental acceptance of the new vaccine, reasons for not receiving vaccine, and the impact of HPV disease knowledge level on vaccine acceptance.

Results

The first cohort of 16–18-year-old girls in 2008 resulted in a 66% uptake rate of the first dose. The subsequent vaccine administration to 16-year-old female cohorts in 2009 and 2010 resulted in first-dose uptake rates of 92% and 91%, respectively. In all the three cohorts, approximately 95% of the girls who had received a first dose completed the full series of three doses (Table 1).

The postvaccination survey achieved a response rate of 90%. Approximately 70% of the responders had some knowledge about HPV and its related diseases and 83% indicated they were very satisfied or satisfied with the new immunization program. Fig. 1 presents the various reasons for not receiving the vaccine.

No serious adverse events were reported during the vaccination period. One vaccine recipient experienced shortness of breath, flushing, and chills immediately after the first dose of vaccine, and one recipient experienced dizziness and fever after the second dose. In both participants, the symptoms resolved without complication.

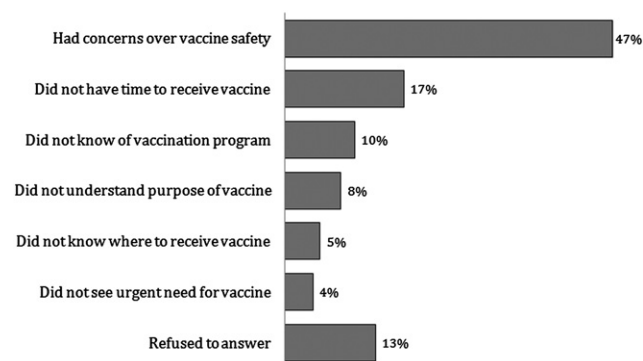


Figure 1 Survey results: reasons for not receiving human papillomavirus (HPV) vaccination. (Respondents could select more than one reason).

Discussion

In Kinmen County, the school-based HPV vaccination uptake rate increased from 66% in 2008 to over 90% in 2009 and 2010. The lower rate of uptake for the first cohort may have been attributed to uncertainty surrounding a newly implemented vaccination program. Excellent vaccine safety and tolerability evidenced in the first cohort may have alleviated public concerns over adverse events from vaccination, leading to significantly higher uptake rates in the subsequent cohorts in 2009 and 2010.

School-based programs have proven to be an effective approach, as target cohorts can be accessed directly through the school system and their parents can be easily contacted for public health education and consent for vaccination. However, older cohorts would unlikely be universally reached through a group vaccination approach, and may need to rely on primary health-care centers for vaccination. In order to maximize vaccine uptake rate, increased and focused effort should be placed on vaccination of the school-age population.

Although the impact of vaccination remains to be observed over the coming decades, early reductions in the rate of cervical abnormalities were reported 3 years after the initiation of the HPV program in Australia.¹⁸ One can confidently predict that, if a high rate of vaccine uptake and regular Pap screenings can be maintained, the incidence of HPV-related diseases including cervical cancer will continue to decline over time in Taiwan.

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References

1. Department of Health, Executive Yuan, Taiwan, ROC. Causes of female cancer deaths over the years. http://www.doh.gov.tw/CHT2006/DM/DM2_2.aspx?now_fod_list_no=11663&class_no=440&level_no=5 [accessed 27.06.12].
2. Bureau of Health Promotion, Department of Health, Executive Yuan, Taiwan, ROC. Taiwan Pap Registry Annual Report 2005–2010. Executive Yuan: Taiwan, ROC.
3. Lin H, Ma YY, Moh JS, Ou YC, Shen SY, ChangChien CC. High prevalence of genital human papillomavirus type 52 and 58 infection in women attending gynecologic practitioners in South Taiwan. *Gynecol Oncol* 2006;101:40–5.
4. Esposito S, Birlutiu V, Jarcuska P, Perino A, Man SC, Vladareanu R, et al. Immunogenicity and safety of human papillomavirus-16/18 AS04-adjuvanted vaccine administered according to an alternative dosing schedule compared with the standard dosing

- schedule in healthy women aged 15 to 25 years: results from a randomized study. *Pediatr Infect Dis J* 2011;**30**:e49–55.
5. Reisinger KS, Block SL, Lazcano-Ponce E, Samakoses R, Esser MT, Erick J, et al. Safety and persistent immunogenicity of a quadrivalent human papillomavirus types 6, 11, 16, 18 L1 virus-like particle vaccine in preadolescents and adolescents: a randomized controlled trial. *Pediatr Infect Dis J* 2007;**26**:201–9.
 6. Dasbach EJ, Insinga RP, Yang YC, Pwu RF, Lac C, Elbasha EH. The cost-effectiveness of a quadrivalent human papillomavirus vaccine in Taiwan. *Asian Pac J Cancer Prev* 2008;**9**:459–66.
 7. Liu PH, Hu FC, Lee PI, Chow SN, Huang CW, Wang JD. Cost-effectiveness of human papillomavirus vaccination for prevention of cervical cancer in Taiwan. *BMC Health Serv Res* 2010;**10**:11.
 8. Liao CH, Liu JT, Pwu RF, You SL, Chow I, Tang CH. Valuation of the economic benefits of human papillomavirus vaccine in Taiwan. *Value Health* 2009;**12**(Suppl. 3):S74–7.
 9. Suárez E, Smith JS, Bosch FX, Nieminen P, Chen CJ, Torvinen S, et al. Cost-effectiveness of vaccination against cervical cancer: a multi-regional analysis assessing the impact of vaccine characteristics and alternative vaccination scenarios. *Vaccine* 2008;**26**(Suppl. 5):F29–45.
 10. Rogoza RM, Ferko N, Bentley J, Meijer CJ, Berkhof J, Wang KL, et al. Optimization of primary and secondary cervical cancer prevention strategies in an era of cervical cancer vaccination: a multi-regional health economic analysis. *Vaccine* 2008;**26**(Suppl. 5):F46–58.
 11. Ogilvie GS, Remple VP, Marra F, McNeil SA, Naus M, Pielak KL, et al. Parental intention to have daughters receive the human papillomavirus vaccine. *CMAJ* 2007;**177**:1506–12.
 12. O'Reilly FW, Cran GW, Stevens AB. Factors affecting influenza vaccine uptake among health care workers. *Occup Med (Lond)* 2005;**55**:474–9.
 13. Brewer NT, Fazekas KI. Predictors of HPV vaccine acceptability: a theory-informed, systematic review. *Prev Med* 2007;**45**:107–14.
 14. Trim K, Nagji N, Elit L, Roy K. Parental knowledge, attitudes, and behaviours towards human papillomavirus vaccination for their children: a systematic review from 2001 to 2011. *Obstet Gynecol Int* 2012;**2012**:921236.
 15. Ault KA. Future II Study Group. Effect of prophylactic human papillomavirus L1 virus-like-particle vaccine on risk of cervical intraepithelial neoplasia grade 2, grade 3, and adenocarcinoma *in situ*: a combined analysis of four randomised clinical trials. *Lancet* 2007;**369**:1861–8.
 16. FUTURE I/II Study Group, Dillner J, Kjaer SK, Wheeler CM, Sigurdsson K, Iversen OE, et al. Four year efficacy of prophylactic human papillomavirus quadrivalent vaccine against low grade cervical, vulvar, and vaginal intraepithelial neoplasia and anogenital warts: randomised controlled trial. *BMJ* 2010;**341**:c3493.
 17. Council of Youth Rights Promotion and Protection, Executive Yuan, Taiwan, ROC. White paper on youth policy agenda. http://ey.cbi.gov.tw/internet/main/doc/doc_detail.aspx?uid=388&docid=1566 [accessed 27.06.12].
 18. Brotherton JM, Fridman M, May CL, Chappell G, Saville AM, Gertig DM. Early effect of the HPV vaccination programme on cervical abnormalities in Victoria, Australia: an ecological study. *Lancet* 2011;**377**:2085–92.